PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Giddings, Peter, John
GLAXOSMITHKLINE
Corporate Intell. Property
(CN925.1)
980 Great West Road
Brentford, Middlesex TW8 9GS
GRANDE BRETAGNE

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	21.05.2004
Applicant's or agent's file reference AS/PG4713 WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/01542	10.04.2003	13.04.2002

Applicant
GLAXO GROUP LIMITED et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Hutterer, G Tel. +49 89 2399-8066

Form PCT/IPEA/416 (January 2004)

Express Mail Label No.
EV332062923US

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
AS/PG4713 WO		

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/01542	10.04.2003	13.04.2002

International Patent Classification (IPC) or both national classification and IPC
A61K9/00, A61K9/00

Applicant
GLAXO GROUP LIMITED et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24.10.2003	21.05.2004

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Luangkhot, N

Telephone No. +49 89 2399-7857

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/01542

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-23 as originally filed

Claims, Numbers

1-27 as originally filed

Drawings, Sheets

1/5-5/5 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 12 regarding industrial applicability

   because:

   ☒ the said international application, or the said claims Nos. 12 regarding industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-2,7-9
	No:	Claims	3-6,10-27
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-27
Industrial applicability (IA)	Yes:	Claims	1-11,13-27
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item I
Basis of the opinion

Serious clarity objections

Claims 15-27, which describe **too many and specific features** that the inhalation device or medicament pack should have, do not fulfil the requirement of Art.6 PCT for lack of clarity because although it is specified that the claimed inhalation device or medicament pack contains the claimed composition (except for claims 24,26-27), **they are directed to a subject-matter which differs from the scope of the subject-matter of present independent composition claim 3**. This makes believe that a **non-unity objection** should be raised.

For further processing, it would be assumed that claims 15-27 are amended into dependent **use** claims such as "**use of a dry powder** pharmaceutical composition according to 3 in an inhalation device or medicament pack comprising .....".

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 12 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V
Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1) The documents cited in the International Search Report (ISR) were numbered respectively from D1-D3; this numbering results from the citation order in the ISR and will be used for the procedure. Unless not specified, the cited passages of each document in the ISR will be considered.

2) D3 is directed to a liquid aerosol formulation and is therefore not relevant for the subject-matter of present application which is concerned with dry powder aerosol composition.

3) Novelty and inventive step according to Art. 33(2) and 33(3) PCT

3a) The subject-matter of claims 1 and 2 is novel because none of the cited prior art describes the use of particulate derivatized carbohydrates in dry powder compositions for inhalation therapy in order to improve stability performance or to eliminate or reduce the detrimental effect on fine particle dose caused on storage of said compositions.
However the said subject-matter does not involve an inventive step because the effects were demonstrated **only** for the compounds described in claims 6 (for example). Therefore the problem which is to improve the stability performance **is likely not to be solved** by the use of **every** derivatized carbohydrates in general, whose notion encompasses too many undefined compounds and does not have a clear and definite meaning.

3b) The subject-matter of claims 3-6 and 14-27 is not novel nor inventive because D1 or D2 describes or suggests a dry powder composition for inhalation therapy and the use of the same in an inhalation device, comprising a/ an active agent, b/ an excipient and c/ a derivatized carbohydrate.

Should claims 15-27, directed to a specific inhalation device and a specific medicinal pack, are made novel and inventive by insisting on their characterizing feature, a non-unity objection would be raised and a search report for the said subject-matter should be established.

It could be argued that neither D1 nor D2 shows with support of comparative tests that the said composition stays stable upon storage with regard to the fine particle fraction (amount of drug recovered in the second stage of the Twin Impinger).

Nevertheless D1 or D2 describes or suggests **an aerosol composition containing a/, b/ and c/. Thus any composition which contains the 3 ingredients would possess automatically and inherently the said performance stability and that is to say the effects described in present application.**

3c) This reasoning applies to the subject-matter of claims 10-13 which is not novel and not inventive because they seem not to contain any features that could confer novelty and/or inventive step to the said subject-matter.

3d) The subject-matter of claim 7 is novel because none of the cited prior art describes a dry powder composition for inhalation therapy comprising a/ an active agent, b/ an excipient and c/ a derivatized carbohydrate, wherein c/ is specifically alpha-D cellobiose octaacetate.

However the said subject-matter does not involve an inventive step because it is considered as an obvious alternative that the skilled man in the art will perform by routine, in order not to interfere with prior art. In the absence of a surprising effect **bound to the use of the specific alpha-D cellobiose octaacetate** compared with the **use of other derivatized carbohydrates of present claim 6**, inventive step cannot be acknowledged.

3e) The subject-matter of claim 8 is novel because none of the cited prior art describes a dry powder composition for inhalation therapy comprising a/ an active agent, b/ an excipient and c/ a derivatized carbohydrate, wherein c/ is present at a concentration of less than 10%.
However the said subject-matter does not involve an inventive step because it is considered as an obvious alternative that the skilled man in the art will perform routinely in order not to interfere with prior art. In the absence comparative tests showing a surprising effect **bound to the specific amount of c/**, inventive step cannot be acknowledged.

3f) The subject-matter of claim 9 is novel because none of the cited prior art describes a dry powder composition for inhalation therapy comprising a/ an active agent, b/ an excipient and c/ a derivatized carbohydrate, wherein c/ has an aerodynamic size in the range of 1-20 micron.
However the said subject-matter does not involve an inventive step because it is considered as an obvious alternative that the skilled man in the art will perform routinely in order not to interfere with prior art. In the absence of comparative tests showing a surprising effect **bound to the specific aerodynamic size of c/**, inventive step cannot be acknowledged.

4) Clarity according to Art. 6 PCT

4a) Independent claims 1 and 2 seem not to meet the requirement of Art. 6 PCT because it appears not to contain all the technical features essential to the invention. The wording "a derivatized carbohydrate" is too broad and does not

have any clear and limited meaning. Therefore the applicant is requested to introduce into independent claims 1 and 2 **the features as described in claims 4 or 5 or 6 or 7 that the said "derivatized carbohydrate" should have.**

4b) Claims 15-27 do not fulfill the requirement of Art. 6 PCT for lack of clarity because according to the wordings thereof, it seems that the **specific device or medicinal pack claims** according to claims 15-27 do not fall, per se, within the scope of the **composition claim** according to claim 3, but seems to rather constitute a **distinguishable subject-matter which can be patentable.**
In order to overcome clarity objection, the applicant is requested to amend the wording of **product claims** 15-27 into a **use claim** of the said composition such as "**use** of the composition of claim 3 **in an** inhalation device or medicinal pack comprising ...".

5) Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description, nor is this document identified therein.

6) For the assessment of the present claim 12 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

7) Any information the applicant may wish to submit concerning the subject-matter of the invention, for example further details of its advantages or of the problem it solves, and for which there is no basis in the application as filed, should be confined to the letter of reply and not be incorporated into the application.

The attention of the applicant is drawn to the fact that the application may not be amended in such a way that it contains subject-matter **which extends beyond the content of the application as filed.**

In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern

amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT). Preferably these indications should be submitted in handwritten form on a copy of the relevant parts of the application as filed.